ehp

LESSON:

Thinking Outside the Box to Estimate Community Drug Use

Summary Students interpret and analyze data from a scientific study that attempted to characterize use of illicit drugs in a community by sampling wastewater and testing for the presence of key metabolites.

Lesson Type **Data Analysis**—students read and interpret data from graphs or figures.

***EHP* Article** Getting Straight on What's Flushed: "Sewage Epidemiology" Measures Community Drug Consumption
Environ Health Perspect 116:A351 (2008)
http://www.ehponline.org/docs/2008/116-8/ss.html#gett

Objectives By the end of this lesson, students should be able to

- interpret data from three different graphs with the same units but with different scales on the *y*-axis
- identify how the body's metabolism of a compound impacts excretion, and what and how much is measured
- describe the concept of a correction factor
- describe how the research reviewed in this lesson can be validated
- describe trends in illicit/street drug use on the basis of metabolites of specific drugs found in wastewater
- identify ways in which the research methods discussed in this lesson could be applied to benefit society

Class Time 50–60 minutes

Grade Level Upper high school, college

Subjects Addressed Biology, Environmental Science, General Science

Aligning with Standards

SKILLS USED OR DEVELOPED

- Comprehension (reading)
- Critical thinking and response
- Graph reading
- Tables and figures (reading)

SPECIFIC CONTENT ADDRESSED

- Correction factors
- Graph reading
- Illicit/street drug use
- Metabolites
- Research methods

NATIONAL SCIENCE EDUCATION STANDARDS MET

Science Content Standards

Unifying Concepts and Processes Standard

- Evidence, models, and explanation
- Form and function
- Change, constancy, and measurement

Science as Inquiry Standard

- Abilities necessary to do scientific inquiry
- Understanding about scientific inquiry

Life Science Standard

- Behavior of organisms

Science and Technology Standard

- Abilities of technical design
- Understanding about science and technology

Science in Personal and Social Perspectives Standard

- Personal and community health
- Natural and human-induced hazards
- Environmental quality
- Science and technology in local, national, and global challenges

History and Nature of Science Standard

- Nature of scientific knowledge

Prepping the Lesson (10 minutes)

INSTRUCTIONS

1. Download and review the article "Getting Straight on What's Flushed: 'Sewage Epidemiology' Measures Community Drug Consumption" at http://www.ehponline.org/docs/2008/116-8/ss.html#gett.
2. Review Background Information, Implementing the Lesson, Assessing the Lesson, and Student Instructions for this lesson.
3. Make copies of the Student Instructions and the article.

MATERIALS (per student)

- 1 copy of "Getting Straight on What's Flushed: 'Sewage Epidemiology' Measures Community Drug Consumption," preferably in color
- 1 copy of the Student Instructions

VOCABULARY

- drug target residue (DTR)
- epidemiology
- forensic science
- illicit/street drugs
- metabolites
- sewage epidemiology

BACKGROUND INFORMATION

The title of the *EHP* summary article "Getting Straight on What's Flushed: 'Sewage Epidemiology' Measures Community Drug Consumption" refers to the science of epidemiology, which investigates the cause, distribution, and control of disease in a population. Although drug addiction is considered a disease, the research (Zuccato et al. 2008) to which the article refers does not look at addiction, just the presence of drugs in wastewater. Therefore, the investigators of the original research study technically did not study a "disease." Thus, epidemiology may not be the best description for this type of research.

The research described in the summary article could potentially be categorized as forensic science, which is concerned with the recognition, collection, identification, and interpretation of physical evidence for criminal/civil law or regulatory purposes. However, forensics has the legal/regulatory end point distinction, and although these new research methods could be used for such, they are not limited to those uses (for example, the presence of illicit/street drugs in sewage could be used for behavioral research).

It is probably not necessary to place too much emphasis on the name of this type of research unless students appear confused by the terminology or need to understand vocabulary to progress with their learning (some students can obtain broad conceptual understanding without becoming caught up in the vocabulary).

Although this lesson takes students through many of the steps and thought processes used in the original research study, it is important for the teacher to be aware of the steps taken by the original study authors to obtain the *y*-axis unit of "estimated drug consumption, mg [milligrams]/day/1,000 people," which is used on the graphs in Step 4 of the Student Instructions. To obtain this unit, the authors:

- collected wastewater samples every 20 minutes for 24 hours, pooled subsamples of each sample, and measured the metabolite concentration per given amount of water;
- multiplied the metabolite amount by the amount of wastewater flowing into the treatment plant (liters/day);
- normalized the data for the population size being served by the treatment plant (a larger treatment plant serving more people has more wastewater entering it), which resulted in the amount of metabolite per day per 1,000 people (the authors assumed that there were no major losses/leaks of wastewater on the way to the plant); and

- back-calculated to estimate the milligrams of actual drug used per day per 1,000 people (mg/day/1,000 people) by multiplying the amount of drug metabolites found in the wastewater by a correction factor that accounts for the different rates at which drugs are excreted by the body (an example from the original research article is provided below):

  "[A]bout 45% of intranasal cocaine (molecular weight 303) is excreted in urine as benzoylecgonine (BE; molecular weight 289), so a measured BE excretion rate of 100 mg/day/1,000 people corresponds to $100/0.45 \times 303/289 = 233$ mg of cocaine consumed per day per 1,000 people."

It is important to note that the unit *mg/day/1,000 peopl*e does not characterize the number of people actually using the drug nor the average dose per user. Thus, there may be a lot of a drug used by a few people or a little bit of drug used by a lot of people, and that usage may vary by region or neighborhood. Because this is a new research technique, the authors are investigating the validity of the technique to characterize drug use by an entire community/city (e.g., comparing drug use in London with Milan on a per-capita basis). As the method develops and becomes more sophisticated, it may eventually be able to characterize finer details about drug use within a given city.

Reference

Zuccato E, Chiabrando C, Castiglioni S, Bagnati R, Fanelli R. 2008. Estimating community drug abuse by wastewater analysis. *Environ Health Perspect* 116:1027–1032. http://www.ehponline.org/members/2008/11022/11022.html

RESOURCES

Environmental Health Perspectives, Environews by Topic page, http://ehp.niehs.nih.gov/. Choose Pharmaceuticals/Drug Abuse

Implementing the Lesson

INSTRUCTIONS

1. Distribute the article "Getting Straight on What's Flushed: 'Sewage Epidemiology' Measures Community Drug Consumption" and the Student Instructions to each student.

2. Discuss the vocabulary and content of the article as needed to help the students understand the following ideas:
   - The article summarizes a new research method to characterize use of illicit/street drugs in cities. The method measures the quantity of drug metabolites in the wastewater.
   - Students do not need to know details about the analytical methods and equipment used in the original research article (e.g., liquid chromatography–tandem mass spectrometry), but it may be helpful to inform them that every type of chemical has a unique "signature," or "spectrum." The equipment referred to in the article helps scientists determine what chemicals are present in the wastewater by showing the signature. If students are curious about what spectral signatures look like, they could search online using the words "spectrum," "image," and the drug of interest, such as "cocaine."

3. Have the students complete Steps 2–6 of the Student Instructions. Discuss with students, as needed, to help them read and interpret the graphs and apply the concepts to a larger societal context.

   You may need to briefly review metabolites with students. Step 2 of the Student Instructions provides a brief definition of metabolites, which are the chemicals excreted after the body processes drugs. Students may wonder why the actual drug is sometimes measured (e.g., measuring cocaine in wastewater as an indicator of cocaine use). The reason is that every chemical is metabolized differently by the body. Some chemicals are thoroughly metabolized, with very little of the original chemical passing through; tetrahydrocannabinol (THC), the main psychoactive substance in cannabis/marijuana, is an example of a highly metabolized chemical (it is converted to a variety of metabolites including TCH-OOH). Other drugs are partially metabolized, with large amounts of the original chemical passing through the body. Obviously, even if the body excretes large amounts of the original unmetabolized chemical, significant effects can still occur in the body (e.g., mind-altering effects or physiological effects such as heat-rate changes). Several different chemicals may be excreted after exposure to a single chemical; for example, the authors used two indicators of cocaine: the metabolite benzoylecgonine (BE) and excreted cocaine. Step 3 highlights why the authors of the original study chose specific metabolites/indicators.

4. In Step 6 students are asked to give an example of how the data can be used to benefit society. Depending on your time and interest in the topic, this may lead to interesting conversations with students about the potential to sample waste streams from individual houses for illicit drugs. Would sampling the waste streams of individual houses be a good use of time or money? Would this constitute an invasion of privacy?

Notes & Helpful Hints

- This lesson could be extended into an inquiry-driven ecology lesson in which students investigate the potential impact of the drugs found in the wastewater on plants and animals exposed to the wastewater.
- Some students may wonder about potential errors in the estimates of illicit drug use. Some errors may derive from the following:
  - people flushing drugs down the toilet, which could result in an overestimate of drug use (since the authors use the original form of the drug as an indicator);
  - drug metabolites/residues getting trapped in fecal solids extracted at the treatment plant, which could result in an underestimate of the drug use; and
  - the legal use of morphine as a painkiller.

Assessing the Lesson (steps not requiring teacher feedback are not listed below; see Student Instructions for complete step-by-step instructions)

Step 2

a. **According to these data, there are essentially two different trends regarding when drug use occurs. Describe these trends and use specific drugs/metabolites as examples.**

The two trends are daily drug use and weekend use. Heroin/morphine and cannabis/marijuana appear to be used on a consistent daily basis, with little change on the weekends. Use of cocaine, methamphetamine, Ecstasy (3,4-methylenedioxy-*N*-methylamphetamine), and other amphetamines jumps on the weekends (these may be "party" drugs).

b. **Which drug appears to be used most frequently? The least frequently? Explain your selection.**

Student answers may vary. Just make sure their response is logical and well explained and that they are reading the *y*-axis correctly, as the scales change on each graph. Just looking at the data on the amount of drug metabolites and assuming all the drugs are metabolized at a similar rate in the body, it would appear that cocaine has the highest use since the total drug residues are several hundred grams per day. Other than the large jump on the weekends, it would appear that Ecstasy has the lowest overall use based on the metabolite data. Amphetamines is also a reasonable answer for the least frequently used drug.

Step 3

a. **Which drugs have the highest and lowest "percentage of drug dose excreted as DTR"? List the drug and the percentage.**

Highest: Ecstasy = 65%

Lowest: Cannabis/marijuana = 0.6%

b. **You have learned that DTR refers to the excreted drugs/drug metabolites the study authors have selected to measure. What does the percentage of drug dose excreted as DTR say about the body's metabolism of the two drugs you listed in Step 3a? Use the percentages to support your answer.**

Essentially the body appears to metabolize about 35% of Ecstasy, with 65% of it being excreted in its original chemical form (or close to its original form). On the other hand, THC, the active ingredient in cannabis/marijuana, appears to be a highly metabolized compound. It is metabolized into different chemicals. The most reliable direct metabolite of THC is THC-COOH, although only about 0.6% of the original THC is excreted as THC-COOH.

c. **One of the major goals of this research was to use drug metabolites in wastewater to estimate the actual use of illicit ("street") drugs. If you wanted to use a metabolite to estimate the actual use of these drugs by people, you would have to factor in how the drug is metabolized. Identify the correction factor for the drugs with the highest and lowest percentage of drug dose excreted as DTR for the two drugs you listed in Step 3a.**

The correction factors are

Ecstasy = 1.5

Cannabis/marijuana = 152

d. In general terms, describe how the correction factor relates to the percentage of drug dose excreted as DTR and how the correction factor might be used to provide a more accurate estimate of the use of the drug.

There is an inverse relationship between the correction factor and the percentage of drug dose excreted as DTR; the higher the percentage of drug dose excreted, the lower the correction factor. Conversely, the lower the percentage of drug dose excreted, the higher the correction factor.

The correction factor can be used to provide a more accurate estimate of the use of the drug because it accounts for the reduction of the amount of DTR due to metabolism. The more highly a drug is metabolized by the body, the smaller the amount of DTR, which may lead one to incorrectly conclude that the drug is being used in smaller amounts than it actually is.

Step 4 **a. According to Figure 2, which drugs appear to be used the most and the least, on average, across all three cities? Explain your answer.**

Cannabis/marijuana appears to be used the most, and methamphetamine appears to be used the least.

b. How does your answer for Step 4a compare with the answer you gave in Step 2b? Explain any differences between the two answers.

Student answers may vary some, but make sure the responses and explanations are logical and clearly explained. Using the answers provided as an example, a response may look like:

Based on the data presented in the graphs in Step 2a, it appeared that cocaine had the highest use and either Ecstasy or amphetamines had the lowest overall use. However, once the metabolism of the drug was considered, it appeared that cannabis/marijuana actually had the highest use and methamphetamine the lowest.

c. According to the data presented in Figure 2, which city appears to have the highest overall street drug use?

London

Step 5 **In this study the authors are trying to find a new method to identify street drug use. What can they do to determine whether this method is reliable/accurate? Explain.**

According to the *EHP* summary article the students read, the authors compared their data with "official prevalence-based figures," and their results compared "reasonably well" with the official data. Additional data on metabolism and drug kinetics would help improve accuracy. Students may have other ideas or suggestions that make sense.

Step 6 **If this research method proves reliable, explain one way the data might be used to benefit society.**

Student answers may vary. The article highlights how this research can improve the accuracy of identifying the actual use of illicit drugs in specific communities or cities, as interview data may have limited reliability (people do not want to admit to using illicit drugs). Currently the method is used to examine wastewater at treatment plants, which provides a city-level view. The potential exists to test at a neighborhood or even household level to identify areas that may require police monitoring. Testing water samples at the individual housing level may raise "invasion of privacy" legal issues in the future.

This approach may also be useful in monitoring use of pharmaceutical drugs in a population.

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Give us your feedback! Send comments about this lesson to ehpscienceed@niehs.nih.gov.

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Thinking Outside the Box to Estimate Community Drug Use

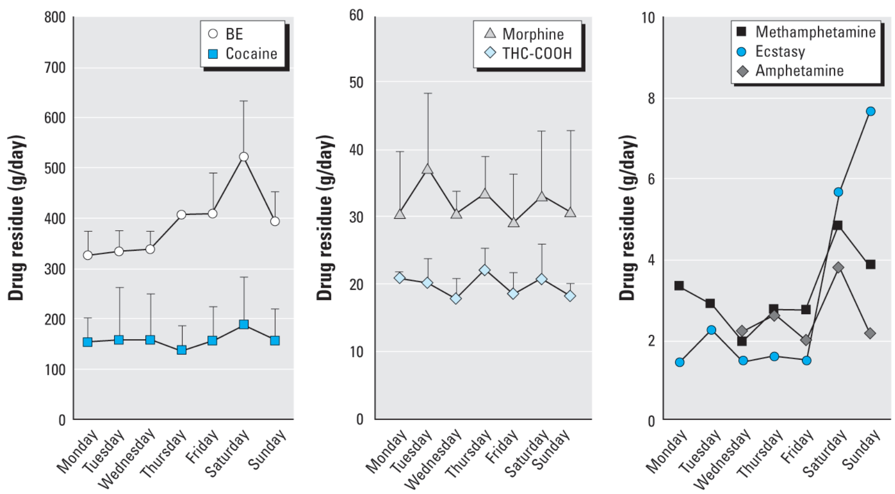
Step 1 Read the article "Getting Straight on What's Flushed: 'Sewage Epidemiology' Measures Community Drug Consumption."

Step 2 Figure 1 below shows a set of graphs from the original research paper described in the article you just read. The authors measured excreted drugs and major drug metabolites, which are chemicals excreted after the body processes the drugs.

- Benzoylecgonine (BE) is a metabolite of cocaine (cocaine can also be excreted largely unchanged).
- Morphine is a metabolite of heroin but can also potentially represent legitimate morphine use in hospitals as painkillers.
- THC-COOH is a metabolite of tetrahydrocannabinol (THC), the active ingredient in cannabis/marijuana.
- Methamphetamine, Ecstasy, and amphetamines are excreted largely unchanged.

Review the graphs (note the different scales used) and answer the questions that follow.

Figure 1



a. According to these data, there are essentially two different trends regarding when drug use occurs. Describe these trends and use specific drugs/metabolites as examples.

National Institute of Environmental Health Sciences

b. Which drug appears to be used most frequently? The least frequently? Explain your selection.

Step 3 The authors selected certain drugs and drug metabolites, which they call "drug target residues (DTRs)," using the following criteria: 1) the DTR is a major and exclusive excretion product of the drug of interest, and 2) the DTR is stable in wastewater (i.e., it does not rapidly break down into still another chemical). These criteria help increase the reliability of the data.

Look at Table 1 below and answer the questions that follow.

Table 1

Drug	DTR	Relation of DTR to parent drug	Percentage of drug dose excreted as DTR[a]	Molar mass ratio (parent drug/DTR)	Correction factor
Cocaine	BE	Major metabolite	45	1.05	2.33
	Cocaine	Parent drug (minor excretion product)			
Heroin	Morphine	Major but nonexclusive metabolite	42	1.29	3.07
	6-Acetylmorphine	Minor but exclusive metabolite			
Amphetamines					
Amphetamine	Amphetamine	Parent drug and major excretion product	30	1.0	3.3
Methamphetamine	Methamphetamine	Parent drug and major excretion product	43	1.0	2.3
Ecstasy	Ecstasy	Parent drug and major excretion product	65	1.0	1.5
Cannabis	THC-COOH	Major metabolite of THC (cannabis active principle)	0.6	0.91	152

a. Which drugs have the highest and lowest percentage of drug dose excreted as DTR? List the drugs and corresponding percentages.

Highest:

Lowest:

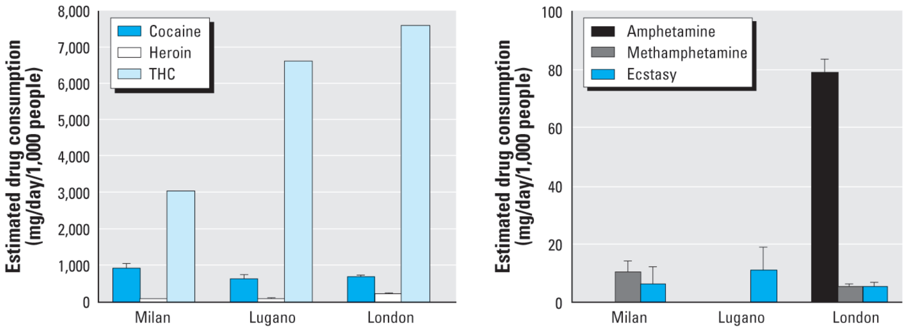
b. You have learned that DTR refers to the excreted drugs/drug metabolites the study authors have selected to measure. What does the percentage of drug dose excreted as DTR say about the body's metabolism of the two drugs you listed in Step 3a? Use the percentages to support your answer.

c. One of the major goals of this research was to use drug metabolites in wastewater to estimate the actual use of illicit ("street") drugs. If you wanted to use a metabolite to estimate the actual use of these drugs by people, you would have to factor in how the drug is metabolized. Identify the correction factor for the drugs with the highest and lowest percentage of drug dose excreted as DTR for the two drugs you listed in Step 3a.

d. In general terms, describe how the correction factor relates to the percentage of drug dose excreted as DTR and how the correction factor might be used to provide a more accurate estimate of the use of the drug.

Step 4 Figure 2 contains two graphs comparing the estimated use of the drugs. These estimates were made using data on the DTRs in the wastewater after incorporating the correction factors listed in Table 1. Review the figure, then answer the questions that follow.

Figure 2



a. According to Figure 2, which drugs appear to be used, on average, the most and the least across all three cities? Explain your answer.

b. How does your answer for Step 4a compare with the answer you gave in Step 2b? Explain any differences between the two answers.

c. According to the data presented in Figure 2, which city appears to have the highest overall street drug use?

Step 5 In this study the authors are trying to find a new method to identify street drug use. What can they do to determine whether this method is reliable/accurate? Explain.

Step 6 If this research method proves reliable, explain one way the data might be used to benefit society.